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Th2-high asthma: a heterogeneous asthma population?

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Background
Airway inflammation in asthma can be subdivided in Th2-high and Th2-low.

Objective
To identify unique patient clusters with a specific airway cytokine expression profile in an unselected population with asthma.

Methods
Induced sputum and clinical records were analysed from 208 asthmatics and 80 healthy individuals. Cytokine-high patients had cytokine mRNA levels above the 90th percentile value in controls. Unsupervised hierarchical clustering was used to determine unique cytokine-based patient clusters.

Results
Cubic Clustering Criterion, pseudo F and t^2 statistics revealed a two- and a six-cluster model. The first cluster (n=23) was found in both models and consists of patients who present with an "IL-5-high and IL-17F-high" profile. Patients with an "IL-4- or IL-13-high" profile did not cluster in one single group. In the six-cluster model, the "IL-17F-low" group was divided into 5 separate clusters: "IL-5-high" profile (n=7), "IFN-γ-high" profile (n=15), "IL-6- and/or TNF-high" profile (n=15), "IL-22-high" profile (n=15) and those patients that were low for all preceding cytokines (n=130; cluster 6). "IL-17F- and IL-5-high" patients had significantly lower FEV_1 and higher sputum neutrophils. Patients that were only "IL-4- or IL-13-high" (cluster 6) had highest F_ENO levels and sputum eosinophils.

Conclusion
Th2-high asthma can be subdivided in patients with "IL-5-high and IL-17F-high" asthma and those with "IL-4- or IL-13-high" asthma. The inflammatory pattern is different between both groups. The former group is characterized by mixed granulocytic airway inflammation whereas the latter group consists of patients with eosinophilic airway inflammation.

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